COMPOSITIONS AND METHODS FOR THE TREATMENT OF NATURAL KILLER CELL RELATED DISEASES

Field of the Invention

The present invention relates to compositions and methods useful for the diagnosis and treatment of immune related diseases.

Background of the Invention

Immune related and inflammatory diseases are the manifestation or consequence of fairly complex, often multiple interconnected biological pathways which in normal physiology are critical to respond to insult or injury, initiate repair from insult or injury, and mount innate and acquired defense against foreign organisms. Disease or pathology occurs when these normal physiological pathways cause additional insult or injury either as directly related to the intensity of the response, as a consequence of abnormal regulation or excessive stimulation, as a reaction to self, or as a combination of these.

Though the genesis of these diseases often involves multistep pathways and often multiple different biological systems/pathways, intervention at critical points in one or more of these pathways can have an ameliorative or therapeutic effect. Therapeutic intervention can occur by either antagonism of a detrimental process/pathway or stimulation of a beneficial process/pathway.

Many immune related diseases are known and have been extensively studied. Such diseases include immune-mediated inflammatory diseases, non-immune-mediated inflammatory diseases, infectious diseases, immunodeficiency diseases, neoplasia, *etc.*

Immune related diseases could be treated by suppressing the immune response. Using neutralizing antibodies that inhibit molecules having immune stimulatory activity would be beneficial in the treatment of immune-mediated and inflammatory diseases. Molecules which inhibit the immune response can be utilized (proteins directly or via the use of antibody agonists) to inhibit the immune response and thus ameliorate immune related disease.

Natural killer (NK) cells are an important effector cell of the innate immune system. They are specialized to effect killing against host cells that have either been infected by viruses, parasites or that have become cancerous. Phenotypically, NK cells are large granular lymphocytes that constitute ~2 % of the circulating lymphocyte population. They are commonly identified by cell surface expression of CD56 and CD16. NK cells mature in the bone marrow from a CD34+ precursor cell that they share with T cells. The mature NK cell, shares expression of CD8, cytolytic machinery, and some KIRs, with T cells, but remains distinct from T cells by the lack of CD3 and the T cell receptors. Like cytotoxic T cells, they contain granules filled with pore forming protein, cytotoxins, serine esterases and proteoglycans that mediate lysis of target cells. Both cytotoxic T cells and NK cells kill on contact by binding to their targets and delivering their lethal burst of chemicals that produces holes in the target cell's membrane. Unlike cytotoxic T cells, NK cells do not need to recognize a specific antigen before initiating lysis. Rather, NK cell activation can be mediated by growth factors and cytokines such as, IL-2, IL-12 and IL-15 have been shown to mediate

proliferative and cytotoxic activities or by a delicate balance between two classes of NK cell receptors, one that activates the cells, and another that inhibits. Killer Ig-like receptors (KIRs) are NK cell receptors that transmit an inhibitory signal if they encounter class I MHC molecules on a cell surface. This is important for killing of both cancerous cells and virally infected cells. Because viruses often suppress class I MHC expression in cells they infect, the virus-infected cell becomes susceptible to killing by NK cells. Likewise, cancer cells have reduced or no class I MHC expression also become susceptible to killing by NK cells. Natural cytotoxicity receptors (NCRs) constitute a family of activating receptors on NK cells. In some effector-target systems, the surface density of NCRs correlates with the cytolytic activity of the NK cells, while in other systems killing requires cooperation between NCR, another activating receptor NKG2D and its adaptor polypeptide DAP10. Additionally, the strength of the stimulatory signals can be influenced by engagement of co-receptors such as 2B4 and NTB-A. The ligands for NCRs and NKG2D, hemoglutanins and MICA, MICB respectively are not expressed by most normal cells, but are induced in most tumor cell lines. Expression of the ligands by tumor cells triggers a dramatic immune response resulting in tumor cell rejection.

Activation of NK cells with IL-15 or IL-12 have been shown to induce both cytotoxic and proliferative effects. Junctional adhesion molecule 2 (JAM2) has been shown to bind to NK cells and has been hypothesized to play a role in lymphocyte extravasation to sites of inflammation. Therefore, a DNA microarray experiment comparing differential expression of genes from these three modes of activation versus resting NK cells has the potential to reveal novel genes or novel gene associations with NK cell activity. Therapeutic antibodies, peptides or small molecules could be developed to target specific genes revealed by these microarrays for the treatment of immune mediated inflammatory diseases and malignancies.

Despite the above research in NK cells, there is a great need for additional diagnostic and therapeutic agents capable of detecting the presence of NK cell mediated disorders in a mammal and for effectively reducing these disorders. Accordingly, it is an objective of the present invention to identify polypeptides that are differentially expressed in activated NK cells as compared to resting NK cells, and to use those polypeptides, and their encoding nucleic acids, to produce compositions of matter useful in the therapeutic treatment and diagnostic detection of NK cell mediated disorders in mammals.

Summary of the Invention

A. Embodiments

The present invention concerns compositions and methods useful for the diagnosis and treatment of immune related disease in mammals, including humans. The present invention is based on the identification of proteins (including agonist and antagonist antibodies) which are a result of stimulation of the immune response in mammals. Immune related diseases can be treated by suppressing or enhancing the immune response. Molecules that enhance the immune response stimulate or potentiate the immune response to an antigen. Molecules which stimulate the immune response can be used therapeutically where enhancement of the immune response would be beneficial. Alternatively, molecules that suppress the immune response attenuate or reduce the immune response to an antigen (*e.g.*, neutralizing antibodies) can be used therapeutically where attenuation of the immune response would be beneficial (*e.g.*, inflammation).

Accordingly, the PRO polypeptides, agonists and antagonists thereof are also useful to prepare medicines and medicaments for the treatment of immune-related and inflammatory diseases. In a specific aspect, such medicines and medicaments comprise a therapeutically effective amount of a PRO polypeptide, agonist or antagonist thereof with a pharmaceutically acceptable carrier. Preferably, the admixture is sterile.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists to a PRO polypeptide which comprises contacting the PRO polypeptide with a candidate molecule and monitoring a biological activity mediated by said PRO polypeptide. Preferably, the PRO polypeptide is a native sequence PRO polypeptide. In a specific aspect, the PRO agonist or antagonist is an anti-PRO antibody.

In another embodiment, the invention concerns a composition of matter comprising a PRO polypeptide or an agonist or antagonist antibody which binds the polypeptide in admixture with a carrier or excipient. In one aspect, the composition comprises a therapeutically effective amount of the polypeptide or antibody. In another aspect, when the composition comprises an immune stimulating molecule, the composition is useful for: (a) increasing infiltration of inflammatory cells into a tissue of a mammal in need thereof, (b) stimulating or enhancing an immune response in a mammal in need thereof, (c) increasing the proliferation of NK cells in a mammal in need thereof in response to an antigen, (d) stimulating the activity of NK cells or (e) increasing the vascular permeability. In a further aspect, when the composition comprises an immune inhibiting molecule, the composition is useful for: (a) decreasing infiltration of inflammatory cells into a tissue of a mammal in need thereof, (b) inhibiting or reducing an immune response in a mammal in need thereof, (c) decreasing the activity of NK cells or (d) decreasing the proliferation of NK cells in a mammal in need thereof in response to an antigen. In another aspect, the composition comprises a further active ingredient, which may, for example, be a further antibody or a cytotoxic or chemotherapeutic agent. Preferably, the composition is sterile.

In another embodiment, the invention concerns a method of treating an immune related disorder in a mammal in need thereof, comprising administering to the mammal an effective amount of a PRO polypeptide, an agonist thereof, or an antagonist thereto. In a preferred aspect, the immune related disorder is selected from the group consisting of: systemic lupus erythematosis, rheumatoid arthritis, osteoarthritis, juvenile chronic arthritis, spondyloarthropathies, systemic sclerosis, idiopathic inflammatory myopathies, Sjögren's syndrome, systemic vasculitis, sarcoidosis, autoimmune hemolytic anemia, autoimmune thrombocytopenia, thyroiditis, diabetes mellitus, immune-mediated renal disease, demyelinating diseases of the central and peripheral nervous systems such as multiple sclerosis, idiopathic demyelinating polyneuropathy or Guillain-Barré syndrome, and chronic inflammatory demyelinating polyneuropathy, hepatobiliary diseases such as infectious, autoimmune chronic active hepatitis, primary biliary cirrhosis, granulomatous hepatitis, and sclerosing cholangitis, inflammatory bowel disease, gluten-sensitive enteropathy, and Whipple's disease, autoimmune or immune-mediated skin diseases including bullous skin diseases, erythema multiforme and contact dermatitis, psoriasis, allergic diseases such as asthma, allergic rhinitis, atopic dermatitis, food hypersensitivity and urticaria, immunologic diseases of the lung such as eosinophilic pneumonias, idiopathic pulmonary fibrosis and hypersensitivity pneumonitis, transplantation associated diseases including graft rejection and graft -versus-host-disease.

In another embodiment, the invention provides an antibody which specifically binds to any of the above or below described polypeptides. Optionally, the antibody is a monoclonal antibody, humanized antibody, antibody fragment or single-chain antibody. In one aspect, the present invention concerns an isolated antibody which binds a PRO polypeptide. In another aspect, the antibody mimics the activity of a PRO polypeptide (an agonist antibody) or conversely the antibody inhibits or neutralizes the activity of a PRO polypeptide (an antagonist antibody). In another aspect, the antibody is a monoclonal antibody, which preferably has nonhuman complementarity determining region (CDR) residues and human framework region (FR) residues. The antibody may be labeled and may be immobilized on a solid support. In a further aspect, the antibody is an antibody fragment, a monoclonal antibody, a single-chain antibody, or an anti-idiotypic antibody.

In yet another embodiment, the present invention provides a composition comprising an anti-PRO antibody in admixture with a pharmaceutically acceptable carrier. In one aspect, the composition comprises a therapeutically effective amount of the antibody. Preferably, the composition is sterile. The composition may be administered in the form of a liquid pharmaceutical formulation, which may be preserved to achieve extended storage stability. Alternatively, the antibody is a monoclonal antibody, an antibody fragment, a humanized antibody, or a single-chain antibody.

In a further embodiment, the invention concerns an article of manufacture, comprising:

(a) a composition of matter comprising a PRO polypeptide or agonist or antagonist thereof;

(b) a container containing said composition; and

(c) a label affixed to said container, or a package insert included in said container referring to the use of said PRO polypeptide or agonist or antagonist thereof in the treatment of an immune related disease. The composition may comprise a therapeutically effective amount of the PRO polypeptide or the agonist or antagonist thereof.

In yet another embodiment, the present invention concerns a method of diagnosing an immune related disease in a mammal, comprising detecting the level of expression of a gene encoding a PRO polypeptide (a) in a test sample of tissue cells obtained from the mammal, and (b) in a control sample of known normal tissue cells of the same cell type, wherein a higher or lower expression level in the test sample as compared to the control sample indicates the presence of immune related disease in the mammal from which the test tissue cells were obtained.

In another embodiment, the present invention concerns a method of diagnosing an immune disease in a mammal, comprising (a) contacting an anti-PRO antibody with a test sample of tissue cells obtained from the mammal, and (b) detecting the formation of a complex between the antibody and a PRO polypeptide, in the test sample; wherein the formation of said complex is indicative of the presence or absence of said disease. The detection may be qualitative or quantitative, and may be performed in comparison with monitoring the complex formation in a control sample of known normal tissue cells of the same cell type. A larger quantity of complexes formed in the test sample indicates the presence or absence of an immune disease in the mammal from which the test tissue cells were obtained. The antibody preferably carries a detectable label. Complex formation can be monitored, for example, by light microscopy, flow cytometry, fluorimetry, or other techniques known in the art. The test sample is usually obtained from an individual suspected of having a deficiency or abnormality of the immune system.

In another embodiment, the invention provides a method for determining the presence of a PRO polypeptide in a sample comprising exposing a test sample of cells suspected of containing the PRO polypeptide to an anti-PRO antibody and determining the binding of said antibody to said cell sample. In a specific aspect, the sample comprises a cell suspected of containing the PRO polypeptide and the antibody binds to the cell. The antibody is preferably detectably labeled and/or bound to a solid support.

In another embodiment, the present invention concerns an immune-related disease diagnostic kit, comprising an anti-PRO antibody and a carrier in suitable packaging. The kit preferably contains instructions for using the antibody to detect the presence of the PRO polypeptide. Preferably the carrier is pharmaceutically acceptable.

In another embodiment, the present invention concerns a diagnostic kit, containing an anti-PRO antibody in suitable packaging. The kit preferably contains instructions for using the antibody to detect the PRO polypeptide.

In another embodiment, the invention provides a method of diagnosing an immune-related disease in a mammal which comprises detecting the presence or absence or a PRO polypeptide in a test sample of tissue cells obtained from said mammal, wherein the presence or absence of the PRO polypeptide in said test sample is indicative of the presence of an immune-related disease in said mammal.

In another embodiment, the present invention concerns a method for identifying an agonist of a PRO polypeptide comprising:

(a) contacting cells and a test compound to be screened under conditions suitable for the induction of a cellular response normally induced by a PRO polypeptide; and

(b) determining the induction of said cellular response to determine if the test compound is an effective agonist, wherein the induction of said cellular response is indicative of said test compound being an effective agonist.

In another embodiment, the invention concerns a method for identifying a compound capable of inhibiting the activity of a PRO polypeptide comprising contacting a candidate compound with a PRO polypeptide under conditions and for a time sufficient to allow these two components to interact and determining whether the activity of the PRO polypeptide is inhibited. In a specific aspect, either the candidate compound or the PRO polypeptide is immobilized on a solid support. In another aspect, the non-immobilized component carries a detectable label. In a preferred aspect, this method comprises the steps of:

(a) contacting cells and a test compound to be screened in the presence of a PRO polypeptide under conditions suitable for the induction of a cellular response normally induced by a PRO polypeptide; and

(b) determining the induction of said cellular response to determine if the test compound is an effective antagonist.

In another embodiment, the invention provides a method for identifying a compound that inhibits the expression of a PRO polypeptide in cells that normally express the polypeptide, wherein the method comprises contacting the cells with a test compound and determining whether the expression of the PRO polypeptide is inhibited. In a preferred aspect, this method comprises the steps of:

(a) contacting cells and a test compound to be screened under conditions suitable for allowing expression of the PRO polypeptide; and

(b) determining the inhibition of expression of said polypeptide.

In yet another embodiment, the present invention concerns a method for treating an immune-related disorder in a mammal that suffers therefrom comprising administering to the mammal a nucleic acid molecule that codes for either (a) a PRO polypeptide, (b) an agonist of a PRO polypeptide or (c) an antagonist of a PRO polypeptide, wherein said agonist or antagonist may be an anti-PRO antibody. In a preferred embodiment, the mammal is human. In another preferred embodiment, the nucleic acid is administered via *ex vivo* gene therapy. In a further preferred embodiment, the nucleic acid is comprised within a vector, more preferably an adenoviral, adeno-associated viral, lentiviral or retroviral vector.

In yet another aspect, the invention provides a recombinant viral particle comprising a viral vector consisting essentially of a promoter, nucleic acid encoding (a) a PRO polypeptide, (b) an agonist polypeptide of a PRO polypeptide, or (c) an antagonist polypeptide of a PRO polypeptide, and a signal sequence for cellular secretion of the polypeptide, wherein the viral vector is in association with viral structural proteins. Preferably, the signal sequence is from a mammal, such as from a native PRO polypeptide.

In a still further embodiment, the invention concerns an *ex vivo* producer cell comprising a nucleic acid construct that expresses retroviral structural proteins and also comprises a retroviral vector consisting essentially of a promoter, nucleic acid encoding (a) a PRO polypeptide, (b) an agonist polypeptide of a PRO polypeptide or (c) an antagonist polypeptide of a PRO polypeptide, and a signal sequence for cellular secretion of the polypeptide, wherein said producer cell packages the retroviral vector in association with the structural proteins to produce recombinant retroviral particles.

In a still further embodiment, the invention provides a method of increasing the activity of NK cells in a mammal comprising administering to said mammal (a) a PRO polypeptide, (b) an agonist of a PRO polypeptide, or (c) an antagonist of a PRO polypeptide, wherein the activity of NK cells in the mammal is increased.

In a still further embodiment, the invention provides a method of decreasing the activity of NK cells in a mammal comprising administering to said mammal (a) a PRO polypeptide, (b) an agonist of a PRO polypeptide, or (c) an antagonist of a PRO polypeptide, wherein the activity of NK cells in the mammal is decreased.

In a still further embodiment, the invention provides a method of increasing the proliferation of NK cells in a mammal comprising administering to said mammal (a) a PRO polypeptide, (b) an agonist of a PRO polypeptide, or (c) an antagonist of a PRO polypeptide, wherein the proliferation of NK cells in the mammal is increased.

In a still further embodiment, the invention provides a method of decreasing the proliferation of NK cells in a mammal comprising administering to said mammal (a) a PRO polypeptide, (b) an agonist of a PRO polypeptide, or (c) an antagonist of a PRO polypeptide, wherein the proliferation of NK cells in the mammal is decreased.

B. Additional Embodiments

In other embodiments of the present invention, the invention provides vectors comprising DNA encoding any of the herein described polypeptides. Host cell comprising any such vector are also provided. By way of example, the host cells may be CHO cells, *E. coli*, or yeast. A process for producing any of the herein described polypeptides is further provided and comprises culturing host cells under conditions

suitable for expression of the desired polypeptide and recovering the desired polypeptide from the cell culture.

In other embodiments, the invention provides chimeric molecules comprising any of the herein described polypeptides fused to a heterologous polypeptide or amino acid sequence. Example of such chimeric molecules comprise any of the herein described polypeptides fused to an epitope tag sequence or a Fc region of an immunoglobulin.

In another embodiment, the invention provides an antibody which specifically binds to any of the above or below described polypeptides. Optionally, the antibody is a monoclonal antibody, humanized antibody, antibody fragment or single-chain antibody.

In yet other embodiments, the invention provides oligonucleotide probes useful for isolating genomic and cDNA nucleotide sequences or as antisense probes, wherein those probes may be derived from any of the above or below described nucleotide sequences.

In other embodiments, the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence that encodes a PRO polypeptide.

In one aspect, the isolated nucleic acid molecule comprises a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity to (a) a DNA molecule encoding a PRO polypeptide having a full-length amino acid sequence as disclosed herein, an amino acid sequence lacking the signal peptide as disclosed herein, an extracellular domain of a transmembrane protein, with or without the signal peptide, as disclosed herein or any other specifically defined fragment of the full-length amino acid sequence as disclosed herein, or (b) the complement of the DNA molecule of (a).

In other aspects, the isolated nucleic acid molecule comprises a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid

sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity to (a) a DNA molecule comprising the coding sequence of a full-length PRO polypeptide cDNA as disclosed herein, the coding sequence of a PRO polypeptide lacking the signal peptide as disclosed herein, the coding sequence of an extracellular domain of a transmembrane PRO polypeptide, with or without the signal peptide, as disclosed herein or the coding sequence of any other specifically defined fragment of the full-length amino acid sequence as disclosed herein, or (b) the complement of the DNA molecule of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity to (a) a DNA molecule that encodes the same mature polypeptide encoded by any of the human protein cDNAs as disclosed herein, or (b) the complement of the DNA molecule of (a).

Another aspect the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence encoding a PRO polypeptide which is either transmembrane domain-deleted or transmembrane domain-inactivated, or is complementary to such encoding nucleotide sequence, wherein the transmembrane domain(s) of such polypeptide are disclosed herein. Therefore, soluble extracellular domains of the herein described PRO polypeptides are contemplated.

Another embodiment is directed to fragments of a PRO polypeptide coding sequence, or the complement thereof, that may find use as, for example, hybridization probes, for encoding fragments of a PRO polypeptide that may optionally encode a polypeptide comprising a binding site for an anti-PRO antibody or as antisense oligonucleotide probes. Such nucleic acid fragments are usually at least about 20 nucleotides in length, alternatively at least about 30 nucleotides in length, alternatively at least about 40 nucleotides in length, alternatively at least about 50 nucleotides in length, alternatively at least about 60 nucleotides in length, alternatively at least about 70 nucleotides in length, alternatively at least about 80 nucleotides in length, alternatively at least about 90 nucleotides in length, alternatively at least about 100 nucleotides in length, alternatively at least about 110 nucleotides in length, alternatively at least about 120 nucleotides in length, alternatively at least about 130 nucleotides in length, alternatively at least about 140 nucleotides in length, alternatively at least about 150 nucleotides in length, alternatively at least about 160

nucleotides in length, alternatively at least about 170 nucleotides in length, alternatively at least about 180 nucleotides in length, alternatively at least about 190 nucleotides in length, alternatively at least about 200 nucleotides in length, alternatively at least about 250 nucleotides in length, alternatively at least about 300 nucleotides in length, alternatively at least about 350 nucleotides in length, alternatively at least about 400 nucleotides in length, alternatively at least about 450 nucleotides in length, alternatively at least about 500 nucleotides in length, alternatively at least about 600 nucleotides in length, alternatively at least about 700 nucleotides in length, alternatively at least about 800 nucleotides in length, alternatively at least about 900 nucleotides in length and alternatively at least about 1000 nucleotides in length, wherein in this context the term "about" means the referenced nucleotide sequence length plus or minus 10% of that referenced length. It is noted that novel fragments of a PRO polypeptide-encoding nucleotide sequence may be determined in a routine manner by aligning the PRO polypeptide-encoding nucleotide sequence with other known nucleotide sequences using any of a number of well known sequence alignment programs and determining which PRO polypeptide-encoding nucleotide sequence fragment(s) are novel. All of such PRO polypeptide-encoding nucleotide sequences are contemplated herein. Also contemplated are the PRO polypeptide fragments encoded by these nucleotide molecule fragments, preferably those PRO polypeptide fragments that comprise a binding site for an anti-PRO antibody.

In another embodiment, the invention provides isolated PRO polypeptide encoded by any of the isolated nucleic acid sequences herein above identified.

In a certain aspect, the invention concerns an isolated PRO polypeptide, comprising an amino acid sequence having at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity, alternatively at least about 84% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to a PRO polypeptide having a full-length amino acid sequence as disclosed herein, an amino acid sequence lacking the signal peptide as disclosed herein, an extracellular domain of a transmembrane protein, with or without the signal peptide, as disclosed herein or any other specifically defined fragment of the full-length amino acid sequence as disclosed herein.

In a further aspect, the invention concerns an isolated PRO polypeptide comprising an amino acid sequence having at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity, alternatively at least about 84% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid

sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to an amino acid sequence encoded by any of the human protein cDNAs as disclosed herein.

In a specific aspect, the invention provides an isolated PRO polypeptide without the N-terminal signal sequence and/or the initiating methionine and is encoded by a nucleotide sequence that encodes such an amino acid sequence as herein before described. Processes for producing the same are also herein described, wherein those processes comprise culturing a host cell comprising a vector which comprises the appropriate encoding nucleic acid molecule under conditions suitable for expression of the PRO polypeptide and recovering the PRO polypeptide from the cell culture.

Another aspect the invention provides an isolated PRO polypeptide which is either transmembrane domain-deleted or transmembrane domain-inactivated. Processes for producing the same are also herein described, wherein those processes comprise culturing a host cell comprising a vector which comprises the appropriate encoding nucleic acid molecule under conditions suitable for expression of the PRO polypeptide and recovering the PRO polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO polypeptide as defined herein. In a particular embodiment, the agonist or antagonist is an anti-PRO antibody or a small molecule.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists to a PRO polypeptide which comprise contacting the PRO polypeptide with a candidate molecule and monitoring a biological activity mediated by said PRO polypeptide. Preferably, the PRO polypeptide is a native PRO polypeptide.

In a still further embodiment, the invention concerns a composition of matter comprising a PRO polypeptide, or an agonist or antagonist of a PRO polypeptide as herein described, or an anti-PRO antibody, in combination with a carrier. Optionally, the carrier is a pharmaceutically acceptable carrier.

Another embodiment of the present invention is directed to the use of a PRO polypeptide, or an agonist or antagonist thereof as herein before described, or an anti-PRO antibody, for the preparation of a medicament useful in the treatment of a condition which is responsive to the PRO polypeptide, an agonist or antagonist thereof or an anti-PRO antibody.

BRIEF DESCRIPTION OF THE DRAWINGS

In the list of figures for the present application, specific cDNA sequences which are differentially expressed in activated Natural Killer (NK) cells as compared to normal resting NK cells are individually identified with a specific alphanumerical designation. These cDNA sequences are differentially expressed in NK cells that are specifically treated as described in Example 1 below. If start and/or stop

codons have been identified in a cDNA sequence shown in the attached figures, they are shown in bold and underlined font, and the encoded polypeptide is shown in the next consecutive figure.

The Figures 1-1477 show the nucleic acids of the invention and their encoded PRO polypeptides. Also included, for convenience is a List of Figures attached hereto as Appendix A, which gives the figure number and the corresponding DNA or PRO number.

List of Figures

Figure 105: PRO4912
Figure 106A-B: DNA274141, AF205218, 201362_at
Figure 107: PRO62077
Figure 108A-B: DNA331291, AB020657, 201363_s_at
Figure 109: PRO62077
Figure 110: DNA329107, NP_008818.3, 201367_s_at
Figure 111: PRO84754
Figure 112A-B: DNA329108, 1383643.16, 201368_at
Figure 113: PRO84755
Figure 114: DNA329107, ZFP36L2, 201369_s_at
Figure 115: PRO84754
Figure 116: DNA329939, 1393503.1, 201417_at
Figure 117: PRO85248
Figure 118: DNA226600, NP_003371.1, 201426_s_at
Figure 119: PRO37063
Figure 120: DNA272286, NP_001743.1, 201432_at
Figure 121: PRO60544
Figure 122: DNA325704, NP_004981.2, 201475_x_at
Figure 123: PRO82188
Figure 124: DNA327551, NP_001024.1, 201477_s_at
Figure 125: PRO59289
Figure 126: DNA304459, BC005020, 201489_at
Figure 127: PRO37073
Figure 128: DNA304459, NP_005720.1, 201490_s_at
Figure 129: PRO37073
Figure 130: DNA323741, NP_003123.1, 201516_at
Figure 131: PRO80498
Figure 132: DNA331292, NP_002779.1, 201532_at
Figure 133: PRO84262
Figure 134: DNA272171, NP_002379.2, 201555_at
Figure 135: PRO60438
Figure 136: DNA227071, NP_000260.1, 201577_at
Figure 137: PRO37534
Figure 138A-B: DNA329944, AB032988, 201581_at
Figure 139: DNA272904, NP_006784.1, 201619_at
Figure 140: PRO60991
Figure 141: DNA329115, NP_434702.1, 201631_s_at
Figure 142: PRO84760
Figure 143A-B: DNA331293, AB011155, 201681_s_at
Figure 144: DNA270883, NP_001061.1, 201714_at
Figure 145: PRO59218
Figure 146: DNA327559, NP_058432.1, 201752_s_at
Figure 147: PRO83589
Figure 148: DNA331294, ADD3, 201753_s_at
Figure 149: PRO86393
Figure 150: DNA227035, NP_006730.1, 201755_at
Figure 151: PRO37498
Figure 152: DNA287167, NP_006627.1, 201761_at
Figure 153: PRO59136
Figure 154: DNA329952, NET1, 201830_s_at
Figure 155: PRO85256
Figure 156: DNA329118, NP_068660.1, 201853_s_at
Figure 157: PRO83123
Figure 158A-B: DNA331295, NP_002710.1, 201877_s_at
Figure 159: PRO86394
Figure 160: DNA150805, NP_055703.1, 201889_at
Figure 161: PRO11583
Figure 162: DNA253582, DNA253582, 201890_at
Figure 163: PRO49181
Figure 164: DNA329956, NP_000875.1, 201892_s_at
Figure 165: PRO85260
Figure 166: DNA328431, NP_001817.1, 201897_s_at
Figure 167: PRO45093
Figure 168: DNA227112, NP_006397.1, 201923_at
Figure 169: PRO37575
Figure 170: DNA275240, NP_005906.2, 201930_at
Figure 171: PRO62927
Figure 172: DNA274167, NP_006422.1, 201946_s_at
Figure 173: PRO62097
Figure 174: DNA275214, NP_002473.1, 201970_s_at
Figure 175: PRO62908
Figure 176: DNA88666, NP_002334.1, 202018_s_at
Figure 177: PRO2892
Figure 178A-B: DNA225991, NP_000518.1, 202068_s_at
Figure 179: PRO36454
Figure 180: DNA327567, NP_005521.1, 202069_s_at
Figure 181: PRO83596
Figure 182A-B: DNA269686, NP_002994.1, 202083_s_at
Figure 183: PRO58096
Figure 184: DNA328440, NP_004517.1, 202107_s_at
Figure 185: PRO84274
Figure 186A-B: DNA304990, NP_006394.1, 202150_s_at
Figure 187: PRO71288
Figure 188: DNA328442, NP_006078.2, 202154_x_at
Figure 189: PRO84275
Figure 190: DNA328444, MGC14458, 202246_s_at
Figure 191: PRO84277
Figure 192: DNA304716, NP_510867.1, 202284_s_at
Figure 193: PRO71142
Figure 194: DNA270142, NP_005947.2, 202309_at
Figure 195: PRO58531
Figure 196: DNA328448, NP_000777.1, 202314_at
Figure 197: PRO62362
Figure 198: DNA331296, UNG, 202330_s_at
Figure 199: PRO86395
Figure 200: DNA325115, NP_001435.1, 202345_s_at
Figure 201: PRO81689
Figure 202: DNA331297, MXI1, 202364_at
Figure 203: PRO86396
Figure 204A-B: DNA150955, NP_036420.1, 202369_s_at
Figure 205: PRO12559
Figure 206: DNA290234, NP_002914.1, 202388_at
Figure 207: PRO70333
Figure 208: DNA66487, NP_002458.1, 202431_s_at
Figure 209: PRO1213
Figure 210: DNA325532, NP_009104.1, 202458_at
Figure 211: PRO307

Figure 212A-B: DNA269642, NP_004557.1, 202464_s_at
Figure 213: PRO58054
Figure 214: DNA227921, NP_003789.1, 202468_s_at
Figure 215: PRO38384
Figure 216: DNA329123, NP_002873.1, 202483_s_at
Figure 217: PRO84765
Figure 218A-B: DNA103449, NP_008862.1, 202497_x_at
Figure 219: PRO4776
Figure 220A-B: DNA103449, SLC2A3, 202499_s_at
Figure 221: PRO4776
Figure 222: DNA234442, NP_055551.1, 202503_s_at
Figure 223: PRO38852
Figure 224A-B: DNA277809, NP_055582.1, 202524_s_at
Figure 225: PRO64556
Figure 226A-B: DNA255105, NP_000850.1, 202539_s_at
Figure 227: PRO50187
Figure 228A-B: DNA255105, HMGCR, 202540_s_at
Figure 229: PRO50187
Figure 230: DNA275244, DNA275244, 202557_at
Figure 231: DNA329979, NP_001062.1, 202589_at
Figure 232: PRO82821
Figure 233: DNA274881, NP_001896.1, 202613_at
Figure 234: PRO62626
Figure 235: DNA59763, NP_000192.1, 202637_s_at
Figure 236: PRO160
Figure 237: DNA59763, ICAM1, 202638_s_at
Figure 238: PRO160
Figure 239: DNA254129, NP_006001.1, 202655_at
Figure 240: PRO49244
Figure 241: DNA326896, NP_003672.1, 202671_s_at
Figure 242: PRO69486
Figure 243: DNA274690, NP_008869.1, 202690_s_at
Figure 244: PRO62479
Figure 245: DNA331298, NP_055271.2, 202730_s_at
Figure 246: PRO81909
Figure 247: DNA331299, PDCD4, 202731_at
Figure 248: PRO86397
Figure 249: DNA150713, NP_006570.1, 202735_at
Figure 250: PRO12082
Figure 251A-B: DNA328464, 977954.20, 202769_at
Figure 252: PRO84290
Figure 253: DNA226578, NP_004345.1, 202770_s_at
Figure 254: PRO37041
Figure 255: DNA273346, NP_055316.1, 202779_s_at
Figure 256: PRO61349
Figure 257A-B: DNA226364, NP_001612.1, 202820_at
Figure 258: PRO36827
Figure 259: DNA329988, NP_036460.1, 202843_at
Figure 260: PRO1471
Figure 261: DNA328483, NP_061163.1, 202911_at
Figure 262: PRO84309
Figure 263: DNA331300, BIN1, 202931_x_at
Figure 264: PRO86398
Figure 265A-B: DNA331301, NP_005424.1, 202932_at
Figure 266: PRO12922
Figure 267A-B: DNA331302, YES1, 202933_s_at
Figure 268: PRO12922
Figure 269: DNA329134, BC012085, 202951_at
Figure 270: PRO59254
Figure 271A-B: DNA328473, NP_006473.1, 202968_s_at
Figure 272: PRO84299
Figure 273A-B: DNA194837, NP_055714.1, 202975_s_at
Figure 274: PRO24100
Figure 275A-B: DNA194837, RHOBTB3, 202976_s_at
Figure 276: PRO24100
Figure 277: DNA329136, NP_057475.1, 203023_at
Figure 278: PRO84772
Figure 279A-B: DNA271865, NP_055566.1, 203037_s_at
Figure 280: PRO60145
Figure 281: DNA269918, NP_003633.1, 203138_at
Figure 282: PRO58316
Figure 283A-B: DNA331303, NP_003129.1, 203181_x_at
Figure 284: PRO86399
Figure 285: DNA331304, BC015747, 203221_at
Figure 286: PRO84167
Figure 287: DNA328294, NP_005068.2, 203222_s_at
Figure 288: PRO84167
Figure 289A-C: DNA274481, NP_000323.1, 203231_s_at
Figure 290: PRO62384
Figure 291A-C: DNA274481, SCA1, 203232_s_at
Figure 292: PRO62384
Figure 293: DNA76514, NP_000409.1, 203233_at
Figure 294: PRO2540
Figure 295: DNA327590, NP_003355.1, 203234_at
Figure 296: PRO83608
Figure 297: DNA325507, NP_005842.1, 203252_at
Figure 298: PRO69461
Figure 299: DNA302020, NP_005564.1, 203276_at
Figure 300: PRO70993
Figure 301A-B: DNA331305, NP_055716.1, 203286_at
Figure 302: PRO86400
Figure 303: DNA271959, NP_002885.1, 203344_s_at
Figure 304: PRO60234
Figure 305: DNA324514, NP_002349.1, 203362_s_at
Figure 306: PRO81169
Figure 307: DNA325749, NP_003868.1, 203372_s_at
Figure 308: PRO12839
Figure 309: DNA325749, STATI2, 203373_at
Figure 310: PRO12839
Figure 311: DNA329140, NP_476433.1, 203391_at
Figure 312: PRO84775
Figure 313: DNA323927, NP_005563.1, 203411_s_at
Figure 314: PRO80660

Figure 315: DNA151037, NP_036461.1, 203414_at
Figure 316: PRO12586
Figure 317A-B: DNA256807, NP_057339.1, 203420_at
Figure 318: PRO51738
Figure 319A-B: DNA275186, DNA275186, 203432_at
Figure 320A-B: DNA330010, NP_005721.2, 203445_s_at
Figure 321: PRO85298
Figure 322: DNA331306, NP_001715.1, 203502_at
Figure 323: PRO58024
Figure 324A-B: DNA331307, NP_003096.1, 203509_at
Figure 325: PRO86401
Figure 326A-B: DNA272399, NP_001197.1, 203542_s_at
Figure 327: PRO60653
Figure 328A-B: DNA272399, BTEB1, 203543_s_at
Figure 329: PRO60653
Figure 330: DNA287246, NP_004044.2, 203612_at
Figure 331: PRO69521
Figure 332A-B: DNA331308, BCL2, 203685_at
Figure 333: PRO86402
Figure 334: DNA324183, DPP4, 203716_s_at
Figure 335: PRO80881
Figure 336: DNA196562, HSPCHDP7, 203717_at
Figure 337: PRO25042
Figure 338: DNA150784, NP_001974.1, 203720_s_at
Figure 339: PRO12800
Figure 340A-B: DNA325369, NP_055877.2, 203737_s_at
Figure 341: PRO81905
Figure 342: DNA275339, NP_005685.1, 203880_at
Figure 343: PRO63012
Figure 344: DNA82376, NP_002407.1, 203915_at
Figure 345: PRO1723
Figure 346: DNA272338, NP_001245.1, 203967_at
Figure 347: PRO60595
Figure 348: DNA272338, CDC6, 203968_s_at
Figure 349: PRO60595
Figure 350: DNA271374, NP_005474.1, 203976_s_at
Figure 351: PRO59673
Figure 352: DNA329145, DUSP4, 204014_at
Figure 353: PRO84780
Figure 354: DNA330034, NP_002907.1, 204023_at
Figure 355: PRO85319
Figure 356: DNA328271, NP_008988.2, 204026_s_at
Figure 357: PRO81868
Figure 358: DNA226737, NP_004576.1, 204070_at
Figure 359: PRO37200
Figure 360A-C: DNA331309, NP_075463.1, 204072_s_at
Figure 361: PRO86403
Figure 362: DNA216689, NP_002975.1, 204103_at
Figure 363: PRO34276
Figure 364: DNA304489, NP_003495.1, 204126_s_at
Figure 365: PRO71058
Figure 366: DNA330037, BC000149, 204127_at
Figure 367: PRO82290
Figure 368: DNA325824, NP_002906.1, 204128_s_at
Figure 369: PRO82290
Figure 370: DNA272655, NP_001818.1, 204170_s_at
Figure 371: PRO60781
Figure 372: DNA226881, NP_002008.2, 204236_at
Figure 373: PRO37344
Figure 374A-B: DNA287273, NP_006435.1, 204240_s_at
Figure 375: PRO69545
Figure 376: DNA228132, NP_076995.1, 204256_at
Figure 377: PRO38595
Figure 378: DNA273802, NP_066950.1, 204285_s_at
Figure 379: PRO61763
Figure 380: DNA273802, PMAIP1, 204286_s_at
Figure 381: PRO61763
Figure 382: DNA331310, NP_000472.1, 204294_at
Figure 383: PRO86404
Figure 384: DNA150972, NP_005252.1, 204472_at
Figure 385: PRO12162
Figure 386A-B: DNA331311, NP_056054.1, 204500_s_at
Figure 387: PRO86405
Figure 388: DNA331312, NP_003600.2, 204504_s_at
Figure 389: PRO82595
Figure 390: DNA225993, NP_000646.1, 204563_at
Figure 391: PRO36456
Figure 392A-B: DNA330054, NP_004746.1, 204633_s_at
Figure 393: PRO85334
Figure 394: DNA103526, LRMP, 204674_at
Figure 395: PRO4853
Figure 396A-B: DNA331313, 481411.2, 204695_at
Figure 397: PRO38036
Figure 398A-B: DNA325192, NP_038203.1, 204744_s_at
Figure 399: PRO81753
Figure 400: DNA330060, NP_002443.2, 204766_s_at
Figure 401: PRO85340
Figure 402: DNA329154, BC000323, 204767_s_at
Figure 403: PRO69568
Figure 404: DNA325479, NP_004102.1, 204768_s_at
Figure 405: PRO69568
Figure 406: DNA330062, NP_006017.1, 204805_s_at
Figure 407: PRO85342
Figure 408: DNA254127, BTN3A3, 204821_at
Figure 409: PRO49242
Figure 410: DNA328544, NP_006673.1, 204834_at
Figure 411: PRO84347
Figure 412: DNA328546, NP_005249.1, 204867_at
Figure 413: PRO84349
Figure 414: DNA329157, NP_004271.1, 204905_s_at
Figure 415: PRO62861
Figure 416: DNA331095, NP_005216.1, 204947_at
Figure 417: PRO86245
Figure 418: DNA325061, NP_005208.1, 205033_s_at

Figure 419: PRO9980
Figure 420: DNA328297, NP_477097.1, 205034_at
Figure 421: PRO59418
Figure 422: DNA324991, ASNS, 205047_s_at
Figure 423: PRO81585
Figure 424: DNA331314, NP_055366.1, 205086_s_at
Figure 425: PRO86406
Figure 426: DNA330074, HUMHM145, 205098_at
Figure 427: PRO85353
Figure 428: DNA226177, NP_001286.1, 205099_s_at
Figure 429: PRO36640
Figure 430: DNA192060, NP_002974.1, 205114_s_at
Figure 431: PRO21960
Figure 432: DNA299899, NP_002148.1, 205133_s_at
Figure 433: PRO62760
Figure 434: DNA273535, NP_004217.1, 205214_at
Figure 435: PRO61515
Figure 436: DNA227081, NP_000390.2, 205249_at
Figure 437: PRO37544
Figure 438A-B: DNA188301, NP_002300.1, 205266_at
Figure 439: PRO21834
Figure 440A-B: DNA331315, LRP8, 205282_at
Figure 441: PRO70090
Figure 442: DNA227173, NP_001456.1, 205285_s_at
Figure 443: PRO37636
Figure 444A-B: DNA331316, 983055.1, 205296_at
Figure 445: PRO86407
Figure 446: DNA325568, NP_001265.1, 205393_s_at
Figure 447: PRO12187
Figure 448: DNA325568, CHEK1, 205394_at
Figure 449: PRO12187
Figure 450: DNA328566, NP_060446.1, 205510_s_at
Figure 451: PRO84363
Figure 452: DNA330085, D86324, 205518_s_at
Figure 453: PRO85359
Figure 454: DNA330086, NP_079184.1, 205519_at
Figure 455: PRO85360
Figure 456: DNA254810, NP_056536.1, 205527_s_at
Figure 457: PRO49906
Figure 458: DNA328567, NP_006797.2, 205548_s_at
Figure 459: PRO84364
Figure 460: DNA329013, NP_005649.1, 205599_at
Figure 461: PRO20128
Figure 462: DNA330088, NP_003087.1, 205644_s_at
Figure 463: PRO61962
Figure 464: DNA330089, NP_004200.2, 205691_at
Figure 465: PRO12507
Figure 466: DNA331317, NP_003636.1, 205768_s_at
Figure 467: PRO51139
Figure 468: DNA331318, SLC27A2, 205769_at
Figure 469: PRO51139
Figure 470: DNA76517, NP_002176.1, 205798_at
Figure 471: PRO2541
Figure 472: DNA194766, NP_079504.1, 205804_s_at
Figure 473: PRO24046
Figure 474A-B: DNA331319, NP_004749.1, 205839_s_at
Figure 475: PRO86408
Figure 476: DNA327651, NP_005612.1, 205863_at
Figure 477: PRO83649
Figure 478: DNA331320, HSU37122, 205882_x_at
Figure 479: PRO86409
Figure 480: DNA287318, NP_002683.1, 205909_at
Figure 481: PRO69583
Figure 482: DNA329166, NP_006518.1, 206052_s_at
Figure 483: PRO84793
Figure 484: DNA329168, CLC, 206207_at
Figure 485: PRO84794
Figure 486: DNA281446, NP_031394.1, 206220_s_at
Figure 487: PRO66285
Figure 488: DNA331321, NP_057473.1, 206245_s_at
Figure 489: PRO86410
Figure 490A-B: DNA331322, NP_055523.1, 206316_s_at
Figure 491: PRO86411
Figure 492: DNA218278, NP_000408.1, 206341_at
Figure 493: PRO34330
Figure 494: DNA329169, NP_002986.1, 206366_x_at
Figure 495: PRO1610
Figure 496A-B: DNA225567, NP_004659.1, 206522_at
Figure 497: PRO36030
Figure 498: DNA227540, NP_003036.1, 206566_at
Figure 499: PRO38003
Figure 500: DNA329171, NP_060246.1, 206583_at
Figure 501: PRO84795
Figure 502: DNA88374, NP_002095.1, 206666_at
Figure 503: PRO2768
Figure 504: DNA330105, HUMNCAX, 206676_at
Figure 505: PRO85372
Figure 506: DNA328590, C6orf32, 206707_x_at
Figure 507: PRO84375
Figure 508: DNA325853, NP_075387.1, 206958_s_at
Figure 509: PRO82315
Figure 510: DNA35629, NP_000586.2, 206975_at
Figure 511: PRO7
Figure 512: DNA188346, NP_001450.1, 206980_s_at
Figure 513: PRO21766
Figure 514A-B: DNA227659, NP_000570.1, 206991_s_at
Figure 515: PRO38122
Figure 516A-B: DNA227750, NP_001550.1, 206999_at
Figure 517: PRO38213
Figure 518: DNA188289, NP_001548.1, 207008_at
Figure 519: PRO21820
Figure 520: DNA255987, NP_004685.1, 207038_at
Figure 521: PRO51038
Figure 522: DNA227481, VAMP1, 207100_s_at
Figure 523: PRO37944
Figure 524: DNA218655, NP_000585.1, 207113_s_at
Figure 525: PRO34451
Figure 526A-B: DNA327674, NP_002739.1, 207121_s_at

Figure 527: PRO83661
Figure 528: DNA331323, NP_001250.1, 207143_at
Figure 529: PRO86412
Figure 530: DNA83048, NP_001916.1, 207269_at
Figure 531: PRO2057
Figure 532: DNA331324, LTB, 207339_s_at
Figure 533: PRO11604
Figure 534: DNA226396, NP_002180.1, 207375_s_at
Figure 535: PRO36859
Figure 536: DNA329178, BTN3A1, 207485_x_at
Figure 537: PRO84801
Figure 538: DNA304473, NP_001552.2, 207536_s_at
Figure 539: PRO2023
Figure 540A-B: DNA330120, FLJ10971, 207606_s_at
Figure 541: PRO85382
Figure 542: DNA227606, NP_001872.2, 207630_s_at
Figure 543: PRO38069
Figure 544: DNA196426, NP_037440.1, 207651_at
Figure 545: PRO24924
Figure 546: DNA256401, NP_004063.1, 207652_s_at
Figure 547: PRO51442
Figure 548: DNA328763, NP_001219.2, 207686_s_at
Figure 549: PRO84511
Figure 550: DNA325654, NP_054752.1, 207761_s_at
Figure 551: PRO4348
Figure 552: DNA329184, CITED2, 207980_s_at
Figure 553: PRO84807
Figure 554: DNA227224, NP_060877.1, 208029_s_at
Figure 555: PRO37687
Figure 556: DNA328610, NP_112601.2, 208146_s_at
Figure 557: PRO84392
Figure 558: DNA325329, NP_004719.1, 208152_s_at
Figure 559: PRO81872
Figure 560: DNA328611, RASGRP2, 208206_s_at
Figure 561: PRO84393
Figure 562: DNA331325, BC006443, 208433_s_at
Figure 563: DNA103427, NP_005239.1, 208438_s_at
Figure 564: PRO4755
Figure 565A-C: DNA331326, ATM, 208442_s_at
Figure 566: PRO86413
Figure 567: DNA331327, NP_036382.2, 208456_s_at
Figure 568: PRO86414
Figure 569: DNA331328, NP_000690.1, 208498_s_at
Figure 570: PRO2157
Figure 571A-B: DNA273567, NP_004944.1, 208625_s_at
Figure 572: PRO61545
Figure 573: DNA329188, BC012142, 208638_at
Figure 574: PRO84810
Figure 575: DNA330139, AK022493, 208657_s_at
Figure 576: PRO85398
Figure 577: DNA304686, NP_002565.1, 208680_at
Figure 578: PRO71112
Figure 579: DNA287189, NP_002038.1, 208693_s_at
Figure 580: PRO69475
Figure 581: DNA330140, AF275798, 208696_at
Figure 582: PRO85399
Figure 583: DNA327696, AF228339, 208763_s_at
Figure 584: PRO83679
Figure 585: DNA238565, NP_005907.2, 208795_s_at
Figure 586: PRO39210
Figure 587: DNA330145, NP_002788.1, 208799_at
Figure 588: PRO84403
Figure 589: DNA273521, NP_002070.1, 208813_at
Figure 590: PRO61502
Figure 591: DNA227874, NP_003320.1, 208864_s_at
Figure 592: PRO38337
Figure 593: DNA328624, BC003562, 208891_at
Figure 594: PRO59076
Figure 595: DNA331329, DUSP6, 208892_s_at
Figure 596: PRO84404
Figure 597: DNA331330, BC005047, 208893_s_at
Figure 598: PRO82215
Figure 599: DNA327701, NP_001203.1, 208910_s_at
Figure 600: PRO82667
Figure 601: DNA226500, NP_005619.1, 208916_at
Figure 602: PRO36963
Figure 603: DNA329552, NP_063948.1, 208925_at
Figure 604: PRO85097
Figure 605: DNA328629, NP_006079.1, 208977_x_at
Figure 606: PRO84407
Figure 607: DNA330154, HUMPECAM27, 208981_at
Figure 608: DNA330155, 7692317.2, 208982_at
Figure 609: PRO85407
Figure 610: DNA328631, AK027318, 209006_s_at
Figure 611: PRO84409
Figure 612: DNA328632, DJ465N24.2.1Homo, 209007_s_at
Figure 613: DNA328635, BC020946, 209026_x_at
Figure 614: PRO84413
Figure 615: DNA274202, NP_006804.1, 209034_at
Figure 616: PRO62131
Figure 617A-C: DNA328637, HSA7042, 209053_s_at
Figure 618: PRO81109
Figure 619: DNA327713, BC010653, 209146_at
Figure 620: PRO37975
Figure 621A-B: DNA328642, AF073310, 209184_s_at
Figure 622: PRO84418
Figure 623: DNA331331, AF161416, 209185_s_at
Figure 624A-B: DNA328643, HUMHK1A, 209186_at
Figure 625: PRO84419
Figure 626: DNA103520, NP_002639.1, 209193_at
Figure 627: PRO4847
Figure 628: DNA226176, NP_003458.1, 209201_x_at
Figure 629: PRO36639
Figure 630: DNA326267, NP_004861.1, 209208_at
Figure 631: PRO82674
Figure 632: DNA328645, NP_009006.1, 209216_at
Figure 633: PRO84421
Figure 634: DNA227483, NP_003120.1, 209218_at
Figure 635: PRO37946
Figure 636: DNA331332, BC007405, 209238_at

Figure 637: PRO86416
Figure 638A-B: DNA331333, 371440.32, 209240_at
Figure 639: PRO86417
Figure 640: DNA328649, NP_116093.1, 209251_x_at
Figure 641: PRO84424
Figure 642: DNA255255, NP_071437.1, 209267_s_at
Figure 643: PRO50332
Figure 644: DNA269750, NP_002919.1, 209324_s_at
Figure 645: PRO58159
Figure 646: DNA269750, RGS16, 209325_s_at
Figure 647: PRO58159
Figure 648: DNA269630, NP_003281.1, 209344_at
Figure 649: PRO58042
Figure 650: DNA330170, AF109161, 209357_at
Figure 651: PRO84807
Figure 652: DNA253811, NP_004410.2, 209457_at
Figure 653: PRO49214
Figure 654: DNA324899, NP_002938.1, 209507_at
Figure 655: PRO81503
Figure 656: DNA328663, NP_057157.1, 209524_at
Figure 657: PRO36183
Figure 658: DNA328663, CGI-142, 209526_s_at
Figure 659: PRO36183
Figure 660A-B: DNA328670, BC001618, 209610_s_at
Figure 661: PRO70011
Figure 662: DNA328599, HSNFKBS, 209636_at
Figure 663: PRO84382
Figure 664: DNA330186, NP_004327.1, 209642_at
Figure 665: PRO85434
Figure 666: DNA330191, NP_036249.1, 209715_at
Figure 667: PRO85439
Figure 668: DNA329178, HSU90552, 209770_at
Figure 669: PRO84801
Figure 670: DNA329205, NP_001343.1, 209782_s_at
Figure 671: PRO84821
Figure 672: DNA226436, NP_001772.1, 209795_at
Figure 673: PRO36899
Figure 674A-B: DNA196499, AB002384, 209829_at
Figure 675: PRO24988
Figure 676: DNA330197, NP_112190.1, 209832_s_at
Figure 677: PRO85445
Figure 678: DNA331334, AF117233, 209845_at
Figure 679: PRO86418
Figure 680: DNA273915, NP_036215.1, 209864_at
Figure 681: PRO61867
Figure 682: DNA330198, AB014719, 209871_s_at
Figure 683: PRO85446
Figure 684: DNA154921, DNA154921, 209967_s_at
Figure 685A-B: DNA227134, NP_000918.1, 209993_at
Figure 686: PRO37597
Figure 687: DNA226658, NP_003736.1, 209999_x_at
Figure 688: PRO37121
Figure 689: DNA226658, SSI-1, 210001_s_at
Figure 690: PRO37121
Figure 691A-B: DNA328685, NP_127497.1, 210113_s_at
Figure 692: PRO34751
Figure 693: DNA330203, NP_003755.1, 210190_at
Figure 694: PRO85449
Figure 695: DNA331335, AF070576, 210202_s_at
Figure 696: DNA217253, NP_000749.1, 210229_s_at
Figure 697: PRO34295
Figure 698: DNA328690, NP_524145.1, 210240_s_at
Figure 699: PRO59660
Figure 700: DNA330206, NP_005801.2, 210288_at
Figure 701: PRO85450
Figure 702: DNA225528, NP_000610.1, 210354_at
Figure 703: PRO35991
Figure 704: DNA331336, TANK, 210458_s_at
Figure 705: PRO86419
Figure 706: DNA329217, BC003406, 210571_s_at
Figure 707: PRO84828
Figure 708: DNA330210, HSU03858, 210607_at
Figure 709: PRO126
Figure 710: DNA331337, TNFSF11, 210643_at
Figure 711: PRO206
Figure 712: DNA227446, NP_003551.1, 210647_x_at
Figure 713: PRO37909
Figure 714: DNA256521, NP_038459.1, 210690_at
Figure 715: PRO51556
Figure 716: DNA331338, AF188298, 210757_x_at
Figure 717: PRO86420
Figure 718: DNA237817, NP_001307.1, 210766_s_at
Figure 719: PRO38923
Figure 720A-B: DNA330216, NP_006445.1, 210778_s_at
Figure 721: PRO85457
Figure 722: DNA188234, NP_000630.1, 210865_at
Figure 723: PRO21942
Figure 724: DNA228132, LCE, 210868_s_at
Figure 725: PRO38595
Figure 726: DNA238565, MCM7, 210983_s_at
Figure 727: PRO39210
Figure 728: DNA326239, NP_006752.1, 210996_s_at
Figure 729: PRO39530
Figure 730: DNA325039, NP_004902.1, 211048_s_at
Figure 731: PRO2733
Figure 732: DNA288254, NP_006000.2, 211058_x_at
Figure 733: PRO69536
Figure 734: DNA288254, TUBA3, 211072_x_at
Figure 735: PRO69536
Figure 736: DNA188234, TNFSF6, 211333_s_at
Figure 737: PRO21942
Figure 738: DNA331339, B3GALT3, 211379_x_at
Figure 739: PRO1074
Figure 740A-B: DNA275066, NP_000170.1, 211450_s_at
Figure 741: PRO62786
Figure 742: DNA331340, HUMCD26A, 211478_s_at
Figure 743: PRO80881
Figure 744: DNA226578, CCNG2, 211559_s_at
Figure 745: PRO37041

Figure 746: DNA331341, AB055881, 211583_x_at
Figure 747: PRO86421
Figure 748: DNA327760, NP_114430.1, 211685_s_at
Figure 749: PRO83729
Figure 750: DNA328706, BC021909, 211714_x_at
Figure 751: PRO10347
Figure 752: DNA329225, EVI2B, 211742_s_at
Figure 753: PRO84833
Figure 754: DNA328649, TUBA6, 211750_x_at
Figure 755: PRO84424
Figure 756: DNA254725, NP_002257.1, 211762_s_at
Figure 757: PRO49824
Figure 758: DNA330226, AF198052, 211794_at
Figure 759: PRO85463
Figure 760: DNA227173, FYB, 211795_s_at
Figure 761: PRO37636
Figure 762A-B: DNA331342, DEFCAP, 211822_s_at
Figure 763: PRO86422
Figure 764: DNA331343, AK026398, 211824_x_at
Figure 765: PRO86423
Figure 766: DNA226881, FLI1, 211825_s_at
Figure 767: PRO37344
Figure 768: DNA226176, CXCR4, 211919_s_at
Figure 769: PRO36639
Figure 770: DNA272286, CAT, 211922_s_at
Figure 771: PRO60544
Figure 772A-B: DNA325227, NP_005338.1, 211936_at
Figure 773: PRO81785
Figure 774A-B: DNA329227, HSRANBP5, 211953_s_at
Figure 775: PRO82307
Figure 776A-C: DNA331344, 1390535.1, 211986_at
Figure 777: PRO86424
Figure 778: DNA287433, NP_006810.1, 212009_s_at
Figure 779: PRO69690
Figure 780: DNA330236, 228447.20, 212071_s_at
Figure 781: PRO85472
Figure 782A-B: DNA150956, BAA06685.1, 212110_at
Figure 783: PRO12560
Figure 784: DNA330240, CAA52801.1, 212141_at
Figure 785: PRO85475
Figure 786: DNA330240, HSP1CDC21, 212142_at
Figure 787A-B: DNA150829, AB014568, 212144_at
Figure 788: DNA324232, NP_005991.1, 212242_at
Figure 789: PRO26228
Figure 790: DNA329182, BC016852, 212259_s_at
Figure 791: PRO84805
Figure 792: DNA150980, HUMMAC30X, 212279_at
Figure 793: DNA150980, DNA150980, 212281_s_at
Figure 794: PRO12566
Figure 795: DNA253017, DNA253017, 212282_at
Figure 796: PRO48926
Figure 797: DNA328719, BC012895, 212295_s_at
Figure 798: PRO84475
Figure 799: DNA271103, NP_005796.1, 212296_at
Figure 800: PRO59425
Figure 801A-B: DNA331345, NP_003596.1, 212307_s_at
Figure 802: PRO59330
Figure 803: DNA326808, BC019307, 212312_at
Figure 804: PRO83141
Figure 805: DNA331346, BC011685, 212330_at
Figure 806: PRO62868
Figure 807: DNA331347, 170995.1, 212334_at
Figure 808: PRO86425
Figure 809A-B: DNA330216, MAD4, 212346_s_at
Figure 810: PRO85457
Figure 811: DNA331348, AF040963, 212347_x_at
Figure 812: PRO85457
Figure 813A-B: DNA330250, NP_060727.1, 212406_s_at
Figure 814: PRO85483
Figure 815: DNA330251, NP_059965.1, 212430_at
Figure 816: PRO85484
Figure 817: DNA269630, TPM4, 212481_s_at
Figure 818: PRO58042
Figure 819A-B: DNA328731, 234169.5, 212500_at
Figure 820: PRO84484
Figure 821: DNA328732, NP_116193.1, 212502_at
Figure 822: PRO84485
Figure 823: DNA226041, NP_005555.1, 212531_at
Figure 824: PRO36504
Figure 825: DNA269882, HSWEE1HU, 212533_at
Figure 826: PRO58280
Figure 827A-D: DNA328737, 148650.1, 212560_at
Figure 828: PRO84490
Figure 829: DNA275100, DNA275100, 212589_at
Figure 830: DNA331349, BC013106, 212590_at
Figure 831: PRO86426
Figure 832: DNA327776, 1379302.1, 212593_s_at
Figure 833: PRO83742
Figure 834: DNA151487, DNA151487, 212594_at
Figure 835: PRO11833
Figure 836: DNA287198, K-ALPHA-1, 212639_x_at
Figure 837: PRO69484
Figure 838: DNA328744, AF318364, 212680_x_at
Figure 839: PRO84496
Figure 840A-B: DNA331350, NP_060903.2, 212689_s_at
Figure 841: PRO86427
Figure 842: DNA273193, DNA273193, 212811_x_at
Figure 843: DNA331351, BC004298, 212823_s_at
Figure 844: DNA254940, BAA91770.1, 213008_at
Figure 845: PRO50030
Figure 846A-B: DNA330275, BAA25487.1, 213045_at
Figure 847: PRO85504
Figure 848: DNA323879, NP_003991.1, 213060_s_at
Figure 849: PRO80622
Figure 850A-B: DNA331352, BAA76818.1, 213088_s_at
Figure 851: PRO86429
Figure 852A-B: DNA331353, AB023191, 213092_x_at

Figure 853A-C: DNA329244, 979567.11, 213106_at
Figure 854: PRO84849
Figure 855: DNA328567, BTG3, 213134_x_at
Figure 856: PRO84364
Figure 857: DNA330277, CAB45152.1, 213142_x_at
Figure 858: PRO85506
Figure 859A-B: DNA329248, BAA20816.1, 213302_at
Figure 860: PRO84850
Figure 861A-B: DNA331354, PPP2R5C, 213305_s_at
Figure 862: PRO86430
Figure 863: DNA155418, DNA155418, 213326_at
Figure 864A-B: DNA331355, AAG24545.1, 213330_s_at
Figure 865: PRO86431
Figure 866: DNA331356, CASP8, 213373_s_at
Figure 867: PRO86432
Figure 868: DNA106195, DNA106195, 213454_at
Figure 869: DNA327795, BC014226, 213457_at
Figure 870: DNA328766, NP_006077.1, 213476_x_at
Figure 871: PRO84514
Figure 872: DNA227483, SQLE, 213562_s_at
Figure 873: PRO37946
Figure 874: DNA327800, 1251176.10, 213575_at
Figure 875: PRO83763
Figure 876: DNA159560, DNA159560, 213577_at
Figure 877: DNA331357, BC010494, 213646_x_at
Figure 878: PRO38556
Figure 879: DNA330293, BC011922, 213666_at
Figure 880: PRO85520
Figure 881: DNA325704, MARS, 213671_s_at
Figure 882: PRO82188
Figure 883: DNA328629, TUBB2, 213726_x_at
Figure 884: PRO84407
Figure 885: DNA328771, HSMYOSIE, 213733_at
Figure 886: DNA150713, EBP, 213787_s_at
Figure 887: PRO12082
Figure 888: DNA330295, NP_037515.1, 213951_s_at
Figure 889: PRO85522
Figure 890: DNA331358, NP_037445.1, 213996_at
Figure 891: PRO86433
Figure 892: DNA329136, HSPC111, 214011_s_at
Figure 893: PRO84772
Figure 894: DNA270687, DNA270687, 214032_at
Figure 895: DNA227224, LC27, 214039_s_at
Figure 896: PRO37687
Figure 897: DNA330298, BC011911, 214095_at
Figure 898: PRO83772
Figure 899: DNA329254, BC004215, 214096_s_at
Figure 900: PRO84854
Figure 901A-B: DNA331359, 332730.12, 214155_s_at
Figure 902: PRO86434
Figure 903: DNA331360, AK022497, 214177_s_at
Figure 904: PRO86435
Figure 905: DNA331361, NP_003318.1, 214228_x_at
Figure 906: PRO2398
Figure 907: DNA331362, AF275719, 214359_s_at
Figure 908: PRO86436
Figure 909: DNA326089, NP_000508.1, 214414_x_at
Figure 910: PRO3629
Figure 911: DNA271374, CHAF1A, 214426_x_at
Figure 912: PRO59673
Figure 913: DNA327811, SHMT2, 214437_s_at
Figure 914: PRO83772
Figure 915: DNA331363, AF001383, 214439_x_at
Figure 916: PRO86437
Figure 917: DNA150971, NP_002249.1, 214470_at
Figure 918: PRO12564
Figure 919: DNA331364, CREM, 214508_x_at
Figure 920: PRO86438
Figure 921: DNA216515, NP_003166.1, 214567_s_at
Figure 922: PRO34267
Figure 923: DNA330303, BAA05499.1, 214662_at
Figure 924: PRO85528
Figure 925: DNA330308, 307914.1, 215029_at
Figure 926: PRO85533
Figure 927: DNA196372, HSBCLXL, 215037_s_at
Figure 928: PRO24874
Figure 929: DNA270522, NP_006013.1, 215111_s_at
Figure 930: PRO58899
Figure 931: DNA330314, 026641.5, 215275_at
Figure 932: PRO85538
Figure 933: DNA328801, 407831.1, 215392_at
Figure 934: PRO84543
Figure 935A-B: DNA331134, NP_003381.1, 215711_s_at
Figure 936: PRO86275
Figure 937A-B: DNA256461, NP_009017.1, 216228_s_at
Figure 938: PRO51498
Figure 939: DNA329266, BC000142, 216237_s_at
Figure 940: PRO12845
Figure 941: DNA88296, NP_005733.1, 216640_s_at
Figure 942: PRO2274
Figure 943: DNA225720, AF151900, 216693_x_at
Figure 944: PRO36183
Figure 945A-B: DNA66475, NP_004439.1, 216836_s_at
Figure 946: PRO1204
Figure 947: DNA331365, NP_004168.1, 216985_s_at
Figure 948: PRO86439
Figure 949: DNA331366, HUMGPCR, 217028_at
Figure 950: PRO4516
Figure 951A-B: DNA331367, BAA34514.1, 217100_s_at
Figure 952: PRO86440
Figure 953: DNA331368, NP_112233.1, 217226_s_at
Figure 954: PRO86441
Figure 955: DNA331369, HSU88968, 217294_s_at
Figure 956: DNA328819, NP_057145.1, 217783_s_at
Figure 957: PRO84557
Figure 958: DNA328303, NP_056525.1, 217807_s_at
Figure 959: PRO84173

Figure 960: DNA227172, NP_066952.1, 217848_s_at
Figure 961: PRO37635
Figure 962: DNA330345, NP_055130.1, 217906_at
Figure 963: PRO85566
Figure 964: DNA227218, NP_003721.2, 217983_s_at
Figure 965: PRO37681
Figure 966: DNA227218, RNASE6PL, 217984_at
Figure 967: PRO37681
Figure 968: DNA328831, NP_057329.1, 217989_at
Figure 969: PRO233
Figure 970: DNA328833, BC018929, 217996_at
Figure 971: PRO84569
Figure 972: DNA328834, AF220656, 217997_at
Figure 973: DNA273008, NP_003972.1, 218009_s_at
Figure 974: PRO61079
Figure 975: DNA328837, NP_057149.1, 218046_s_at
Figure 976: PRO81876
Figure 977: DNA329276, NP_077001.1, 218069_at
Figure 978: PRO12104
Figure 979: DNA330356, NP_006318.1, 218118_s_at
Figure 980: PRO85572
Figure 981: DNA327857, NP_057386.1, 218142_s_at
Figure 982: PRO83799
Figure 983: DNA327858, NP_036473.1, 218238_at
Figure 984: PRO83800
Figure 985: DNA328850, NP_057187.1, 218254_s_at
Figure 986: PRO84581
Figure 987A-B: DNA331370, NP_055101.2, 218266_s_at
Figure 988: PRO11501
Figure 989: DNA331371, NP_060401.1, 218272_at
Figure 990: PRO86442
Figure 991: DNA331372, FLJ20950, 218298_s_at
Figure 992: PRO86443
Figure 993: DNA327862, NP_060445.1, 218349_s_at
Figure 994: PRO83803
Figure 995: DNA328854, NP_056979.1, 218350_s_at
Figure 996: PRO84585
Figure 997: DNA304468, NP_077300.1, 218358_at
Figure 998: PRO71044
Figure 999: DNA328856, NP_068376.1, 218380_at
Figure 1000: PRO84586
Figure 1001: DNA327865, NP_079105.1, 218454_at
Figure 1002: PRO83806
Figure 1003: DNA329286, NP_005691.2, 218567_x_at
Figure 1004: PRO69644
Figure 1005A-B: DNA273435, NP_057532.1, 218585_s_at
Figure 1006: PRO61430
Figure 1007: DNA330377, NP_036577.1, 218638_s_at
Figure 1008: PRO85590
Figure 1009: DNA304835, NP_071327.1, 218681_s_at
Figure 1010: PRO71242
Figure 1011: DNA329288, NP_061910.1, 218695_at
Figure 1012: PRO84880
Figure 1013: DNA326185, FLJ13912, 218719_s_at
Figure 1014: PRO82602
Figure 1015: DNA330381, NP_076958.1, 218741_at
Figure 1016: PRO38668
Figure 1017: DNA331373, NP_075526.1, 218769_s_at
Figure 1018: PRO86444
Figure 1019A-B: DNA327971, NP_006104.3, 218807_at
Figure 1020: PRO83893
Figure 1021: DNA330388, NP_078905.1, 218883_s_at
Figure 1022: PRO85597
Figure 1023: DNA331092, NP_078918.2, 218885_s_at
Figure 1024: PRO86243
Figure 1025: DNA226633, NP_060376.1, 218886_at
Figure 1026: PRO37096
Figure 1027: DNA328881, NP_057706.2, 218890_x_at
Figure 1028: PRO49469
Figure 1029: DNA325622, NP_060518.1, 218894_s_at
Figure 1030: PRO82113
Figure 1031: DNA328364, SIGIRR, 218921_at
Figure 1032: PRO84223
Figure 1033: DNA329050, NP_057053.1, 218982_s_at
Figure 1034: PRO84712
Figure 1035: DNA330391, NP_076999.1, 219000_s_at
Figure 1036: PRO34008
Figure 1037: DNA227187, NP_057703.1, 219014_at
Figure 1038: PRO37650
Figure 1039: DNA329293, NP_057136.1, 219037_at
Figure 1040: PRO84883
Figure 1041: DNA331374, NP_009177.2, 219157_at
Figure 1042: PRO86445
Figure 1043: DNA331375, AK000192, 219168_s_at
Figure 1044: PRO86446
Figure 1045: DNA329223, NP_037517.1, 219183_s_at
Figure 1046: PRO84831
Figure 1047: DNA329296, NP_060328.1, 219258_at
Figure 1048: PRO84886
Figure 1049A-B: DNA331376, NP_079484.1, 219304_s_at
Figure 1050: PRO86447
Figure 1051: DNA287404, NP_073748.1, 219334_s_at
Figure 1052: PRO69661
Figure 1053: DNA331377, NP_060753.1, 219347_at
Figure 1054: PRO86448
Figure 1055: DNA254518, NP_057354.1, 219371_s_at
Figure 1056: PRO49625
Figure 1057: DNA328902, NP_071750.1, 219452_at
Figure 1058: PRO84623
Figure 1059: DNA327890, NP_079021.1, 219493_at
Figure 1060: PRO83826
Figure 1061A-B: DNA227179, NP_059120.1, 219505_at
Figure 1062: PRO37642
Figure 1063: DNA329299, NP_004660.1, 219529_at
Figure 1064: PRO84888
Figure 1065: DNA330410, NP_060925.1, 219555_s_at
Figure 1066: PRO85618

Figure 1067: DNA327891, NP_078909.1, 219563_at
Figure 1068: PRO83827
Figure 1069: DNA331378, ALS2CR8, 219834_at
Figure 1070: PRO86449
Figure 1071: DNA255255, LOC64116, 219869_s_at
Figure 1072: PRO50332
Figure 1073: DNA256325, NP_005470.1, 219889_at
Figure 1074: PRO51367
Figure 1075: DNA328923, NP_075379.1, 219892_at
Figure 1076: PRO84640
Figure 1077: DNA330421, NP_057438.2, 219911_s_at
Figure 1078: PRO85626
Figure 1079: DNA330423, NP_037466.2, 219920_s_at
Figure 1080: PRO85628
Figure 1081: DNA328924, NP_057150.2, 219933_at
Figure 1082: PRO84641
Figure 1083: DNA330537, NP_060533.2, 220085_at
Figure 1084: PRO81892
Figure 1085: DNA227302, NP_037401.1, 220132_s_at
Figure 1086: PRO37765
Figure 1087A-B: DNA328930, NP_038465.1, 220253_s_at
Figure 1088: PRO23525
Figure 1089: DNA330436, NP_037394.1, 220319_s_at
Figure 1090: PRO85639
Figure 1091: DNA327904, NP_071419.2, 220330_s_at
Figure 1092: PRO83839
Figure 1093: DNA331379, PHEMX, 220558_x_at
Figure 1094: PRO86450
Figure 1095: DNA330440, NP_079098.1, 220591_s_at
Figure 1096: PRO85642
Figure 1097: DNA255734, NP_057607.1, 220646_s_at
Figure 1098: PRO50791
Figure 1099A-B: DNA327908, MCM10, 220651_s_at
Figure 1100: PRO83843
Figure 1101: DNA323756, NP_057267.2, 220688_s_at
Figure 1102: PRO80512
Figure 1103: DNA331380, DKFZp566O084Homo, 220690_s_at
Figure 1104: DNA288247, NP_478059.1, 220892_s_at
Figure 1105: PRO70011
Figure 1106: DNA331381, BA108L7.2, 220974_x_at
Figure 1107: PRO86451
Figure 1108: DNA287397, NP_112214.1, 220987_s_at
Figure 1109: PRO69654
Figure 1110: DNA328945, NP_079177.2, 221081_s_at
Figure 1111: PRO84657
Figure 1112: DNA331382, CISH, 221223_x_at
Figure 1113: PRO86452
Figure 1114: DNA330451, NP_110429.1, 221249_s_at
Figure 1115: PRO85652
Figure 1116: DNA328948, NP_110437.1, 221253_s_at
Figure 1117: PRO84659
Figure 1118: DNA326507, NP_112490.2, 221267_s_at
Figure 1119: PRO82879
Figure 1120: DNA329471, NP_110387.1, 221417_x_at
Figure 1121: PRO85036
Figure 1122A-B: DNA329314, 1149046.7, 221478_at
Figure 1123: PRO84902
Figure 1124: DNA227303, NP_004322.1, 221479_s_at
Figure 1125: PRO37766
Figure 1126: DNA326221, NP_057179.1, 221521_s_at
Figure 1127: PRO82634
Figure 1128: DNA330457, NP_076944.1, 221559_s_at
Figure 1129: PRO85658
Figure 1130: DNA329318, IRO033793, 221564_at
Figure 1131: DNA329319, BC006401, 221601_s_at
Figure 1132: PRO1607
Figure 1133: DNA329319, NP_005440.1, 221602_s_at
Figure 1134: PRO1607
Figure 1135: DNA330459, NP_060083.1, 221677_s_at
Figure 1136: PRO50083
Figure 1137: DNA328961, NP_443112.1, 221756_at
Figure 1138: PRO84667
Figure 1139: DNA328961, MGC17330, 221757_at
Figure 1140: PRO84667
Figure 1141: DNA331383, BC007588, 221769_at
Figure 1142: DNA331384, AK026326, 221985_at
Figure 1143: PRO86454
Figure 1144: DNA330467, NP_060114.1, 221986_s_at
Figure 1145: PRO85665
Figure 1146: DNA254739, NP_068766.1, 221987_s_at
Figure 1147: PRO49837
Figure 1148: DNA257797, DNA257797, 222036_s_at
Figure 1149: DNA257798, DNA257798, 222037_at
Figure 1150: DNA325648, NP_037409.2, 222077_s_at
Figure 1151: PRO82139
Figure 1152A-B: DNA331385, AF274889S4, 222088_s_at
Figure 1153: DNA331386, HST000012, 222150_s_at
Figure 1154A-B: DNA331387, NP_008919.2, 222162_s_at
Figure 1155: PRO86456
Figure 1156: DNA328977, NP_071344.1, 222216_s_at
Figure 1157: PRO84678
Figure 1158: DNA325821, BC014334, 222402_at
Figure 1159: PRO82287
Figure 1160A-B: DNA256489, NP_079110.1, 222464_s_at
Figure 1161: PRO51526
Figure 1162: DNA304460, BC003048, 222500_at
Figure 1163: PRO4984
Figure 1164: DNA327942, NP_060596.1, 222642_s_at
Figure 1165: PRO83870
Figure 1166: DNA327943, NP_055399.1, 222646_s_at
Figure 1167: PRO865
Figure 1168A-B: DNA273435, RAMP, 222680_s_at
Figure 1169: PRO61430
Figure 1170: DNA330486, HSM802473, 222692_s_at
Figure 1171: DNA331388, NP_068747.1, 222753_s_at
Figure 1172: PRO3567
Figure 1173: DNA329335, AK023411, 222843_at

Figure 1174: PRO84919
Figure 1175: DNA331389, NP_071428.2, 222848_at
Figure 1176: PRO81238
Figure 1177: DNA287404, FLJ22833, 222872_x_at
Figure 1178: PRO69661
Figure 1179: DNA330500, AK022872, 222889_at
Figure 1180: PRO85693
Figure 1181A-B: DNA287236, AB024334, 222985_at
Figure 1182: PRO10607
Figure 1183: DNA329571, NP_057547.3, 222996_s_at
Figure 1184: PRO51662
Figure 1185: DNA189412, NP_057390.1, 223054_at
Figure 1186: PRO25349
Figure 1187: DNA288247, PSA, 223062_s_at
Figure 1188: PRO70011
Figure 1189: DNA331390, AAF28975.1, 223070_at
Figure 1190: PRO86457
Figure 1191: DNA324209, NP_057018.1, 223096_at
Figure 1192: PRO80902
Figure 1193: DNA330436, MIR, 223129_x_at
Figure 1194: PRO85639
Figure 1195: DNA330513, AF212221, 223130_s_at
Figure 1196: PRO85703
Figure 1197: DNA254276, NP_054896.1, 223180_s_at
Figure 1198: PRO49387
Figure 1199: DNA254416, NP_060915.1, 223209_s_at
Figure 1200: PRO49526
Figure 1201A-B: DNA257461, NP_113607.1, 223217_s_at
Figure 1202: PRO52040
Figure 1203A-B: DNA257461, MAIL, 223218_s_at
Figure 1204: PRO52040
Figure 1205: DNA326056, NP_072088.1, 223264_at
Figure 1206: PRO82491
Figure 1207: DNA330518, BC002493, 223274_at
Figure 1208: PRO85708
Figure 1209: DNA329355, NP_150596.1, 223299_at
Figure 1210: PRO50434
Figure 1211: DNA227125, AF132297, 223377_x_at
Figure 1212: PRO37588
Figure 1213A-B: DNA331391, NP_065947.1, 223464_at
Figure 1214: PRO49998
Figure 1215: DNA329456, NP_057126.1, 223490_s_at
Figure 1216: PRO85023
Figure 1217: DNA330536, NP_115666.1, 223542_at
Figure 1218: PRO85722
Figure 1219: DNA330537, AF155827, 223556_at
Figure 1220: PRO81892
Figure 1221: DNA287253, LOC85028, 223773_s_at
Figure 1222: PRO69527
Figure 1223: DNA327200, NP_114156.1, 223836_at
Figure 1224: PRO1065
Figure 1225: DNA331392, NP_004186.1, 223851_s_at
Figure 1226: PRO364
Figure 1227: DNA331393, D83532, 223961_s_at
Figure 1228: PRO86458
Figure 1229: DNA330552, BC001104, 223984_s_at
Figure 1230: PRO85736
Figure 1231: DNA330558, NP_057588.1, 224330_s_at
Figure 1232: PRO84950
Figure 1233: DNA328323, NP_114148.2, 224428_s_at
Figure 1234: PRO69531
Figure 1235: DNA331394, MGC11316, 224482_s_at
Figure 1236: PRO86459
Figure 1237: DNA327976, NP_116120.1, 224511_s_at
Figure 1238: PRO69574
Figure 1239: DNA329374, NP_115735.1, 224523_s_at
Figure 1240: PRO84953
Figure 1241: DNA331395, TNFRSF18, 224553_s_at
Figure 1242: PRO86460
Figure 1243: DNA331396, 1357555.1, 224603_at
Figure 1244: PRO86461
Figure 1245A-B: DNA327981, 344095.3, 224654_at
Figure 1246: PRO83901
Figure 1247A-B: DNA330574, AB033054, 224698_at
Figure 1248: DNA324173, NP_115766.2, 224714_at
Figure 1249: PRO80871
Figure 1250: DNA257352, DNA257352, 224739_at
Figure 1251: PRO51940
Figure 1252A-B: DNA287330, BAA86479.1, 224799_at
Figure 1253: PRO69594
Figure 1254A-B: DNA287330, AB032991, 224801_at
Figure 1255: DNA331397, AK001723, 224802_at
Figure 1256: PRO23259
Figure 1257A-C: DNA329379, 010205.2, 224847_at
Figure 1258: PRO84957
Figure 1259: DNA257789, NP_116219.1, 224903_at
Figure 1260: PRO52338
Figure 1261: DNA151170, DNA151170, 224989_at
Figure 1262: PRO12626
Figure 1263A-B: DNA327993, 898436.7, 225133_at
Figure 1264: PRO81138
Figure 1265: DNA327996, BC010181, 225195_at
Figure 1266: PRO83915
Figure 1267: DNA329394, BC010416, 225201_s_at
Figure 1268: DNA329396, NP_060866.1, 225253_s_at
Figure 1269: PRO84972
Figure 1270: DNA304802, AAH00967.1, 225439_at
Figure 1271: PRO71212
Figure 1272A-B: DNA330617, 336147.2, 225447_at
Figure 1273: PRO59923
Figure 1274: DNA196561, DNA196561, 225470_at
Figure 1275A-B: DNA331398, 234824.7, 225478_at
Figure 1276: PRO86462
Figure 1277: DNA329405, HSM800962, 225520_at
Figure 1278A-B: DNA330620, CAB55950.1, 225533_at
Figure 1279: PRO85794
Figure 1280: DNA330621, AF116628, 225535_s_at
Figure 1281: DNA328008, 240051.4, 225541_at

Figure 1282: PRO83926
Figure 1283: DNA329406, 1503139.10, 225562_at
Figure 1284: PRO84979
Figure 1285: DNA304469, NP_149078.1, 225621_at
Figure 1286: PRO71045
Figure 1287: DNA331399, 994419.37, 225622_at
Figure 1288: PRO86463
Figure 1289A-B: DNA331400, NP_060910.2, 225626_at
Figure 1290: PRO86464
Figure 1291: DNA329940, NP_001805.1, 225647_s_at
Figure 1292: PRO2679
Figure 1293A-B: DNA288261, NP_037414.2, 225655_at
Figure 1294: PRO70021
Figure 1295A-B: DNA331401, 336865.4, 225700_at
Figure 1296: PRO86465
Figure 1297: DNA304821, BC011254, 225706_at
Figure 1298: DNA254820, DNA254820, 225707_at
Figure 1299: PRO49916
Figure 1300: DNA330633, BC003515, 225723_at
Figure 1301: DNA329417, 411336.1, 225842_at
Figure 1302: PRO84989
Figure 1303A-B: DNA331402, 197159.1, 225845_at
Figure 1304: PRO86466
Figure 1305: DNA287370, BAB14983.1, 225866_at
Figure 1306: PRO69630
Figure 1307A-B: DNA331403, TP53INP1, 225912_at
Figure 1308: PRO86467
Figure 1309A-B: DNA331405, 979005.2, 225956_at
Figure 1310: PRO86468
Figure 1311: DNA328021, BC004538, 226038_at
Figure 1312A-B: DNA329428, 1446144.8, 226218_at
Figure 1313: PRO84999
Figure 1314: DNA193896, DNA193896, 226276_at
Figure 1315: PRO23314
Figure 1316: DNA328028, NP_005773.1, 226319_s_at
Figure 1317: PRO83945
Figure 1318: DNA328028, ALY, 226320_at
Figure 1319: PRO83945
Figure 1320A-B: DNA331406, 399773.27, 226334_s_at
Figure 1321: PRO86470
Figure 1322A-B: DNA331407, 198233.1, 226352_at
Figure 1323: PRO86471
Figure 1324A-B: DNA331409, AB051464, 226370_at
Figure 1325A-B: DNA330675, 177663.2, 226372_at
Figure 1326: PRO85847
Figure 1327: DNA330677, 1384190.6, 226390_at
Figure 1328: PRO85849
Figure 1329: DNA331410, HSM802051, 226416_at
Figure 1330: PRO86474
Figure 1331: DNA330679, BC013040, 226456_at
Figure 1332A-B: DNA330680, BC022792, 226481_at
Figure 1333: PRO85852
Figure 1334: DNA330684, 984114.1, 226548_at
Figure 1335: PRO85855
Figure 1336: DNA257914, DNA257914, 226743_at
Figure 1337: PRO52447
Figure 1338: DNA328038, 216863.2, 226811_at
Figure 1339: PRO83953
Figure 1340: DNA328044, 039170.3, 226936_at
Figure 1341: PRO83958
Figure 1342A-B: DNA330705, 198782.1, 227020_at
Figure 1343: PRO85876
Figure 1344A-B: DNA330706, AF445027, 227027_at
Figure 1345: PRO85877
Figure 1346: DNA331411, 232146.1, 227200_at
Figure 1347: PRO86475
Figure 1348: DNA330715, BC022374, 227212_s_at
Figure 1349: PRO85886
Figure 1350: DNA331412, 1378353.1, 227223_at
Figure 1351: PRO86476
Figure 1352A-B: DNA329442, AH007300S2, 227265_at
Figure 1353: DNA329444, BC017821, 227278_at
Figure 1354: PRO85012
Figure 1355: DNA330718, 025465.3, 227295_at
Figure 1356: PRO85889
Figure 1357A-B: DNA330721, 198680.1, 227350_at
Figure 1358: PRO85892
Figure 1359: DNA226872, NP_001955.1, 227404_s_at
Figure 1360: PRO37335
Figure 1361: DNA329450, BC017226, 227726_at
Figure 1362: PRO85018
Figure 1363: DNA59606, DNA59606, 227803_at
Figure 1364: PRO1107
Figure 1365: DNA329456, RRP40, 227916_x_at
Figure 1366: PRO85023
Figure 1367: DNA330745, BC011716, 228069_at
Figure 1368: PRO85913
Figure 1369: DNA329460, BC017117, 228092_at
Figure 1370: PRO85027
Figure 1371: DNA330436, AF187016, 228098_s_at
Figure 1372: PRO85639
Figure 1373: DNA329461, BC016615, 228113_at
Figure 1374: PRO85028
Figure 1375: DNA331413, 286318.11, 228284_at
Figure 1376: PRO86477
Figure 1377: DNA331414, 1450017.11, 228559_at
Figure 1378: PRO86478
Figure 1379: DNA331415, 345279.19, 228788_at
Figure 1380: PRO86479
Figure 1381: DNA330780, 335374.1, 228955_at
Figure 1382: PRO85944
Figure 1383: DNA330784, 233595.21, 228990_at
Figure 1384: PRO85948
Figure 1385: DNA330787, 349981.7, 229041_s_at
Figure 1386: PRO85951
Figure 1387: DNA327307, AF442769, 229215_at
Figure 1388: PRO83560
Figure 1389: DNA287421, 234832.1, 229437_at

Figure 1390: PRO69678
Figure 1391: DNA330799, 481875.1, 229551_x_at
Figure 1392: PRO85963
Figure 1393A-B: DNA330809, 336997.1, 229844_at
Figure 1394: PRO85973
Figure 1395: DNA329466, AF327346, 230069_at
Figure 1396: PRO23814
Figure 1397A-B: DNA331416, FREQ, 230146_s_at
Figure 1398: PRO11501
Figure 1399: DNA329468, BC011589, 230170_at
Figure 1400: PRO88
Figure 1401: DNA330818, 212282.1, 230304_at
Figure 1402: PRO85982
Figure 1403: DNA257756, DNA257756, 230405_at
Figure 1404: DNA329471, EDG8, 230464_at
Figure 1405: PRO85036
Figure 1406: DNA331417, 333493.3, 230748_at
Figure 1407: PRO86480
Figure 1408: DNA331418, 7693630.2, 230917_at
Figure 1409: PRO86481
Figure 1410A-B: DNA287217, DNA287217, 231259_s_at
Figure 1411: PRO36766
Figure 1412: DNA330843, 201388.1, 231832_at
Figure 1413: PRO86006
Figure 1414: DNA331419, 085942.3, 232001_at
Figure 1415: PRO86482
Figure 1416: DNA331420, 029520.1, 232210_at
Figure 1417: PRO86483
Figure 1418: DNA331421, 1448461.1, 232614_at
Figure 1419: PRO86484
Figure 1420: DNA328194, 998827.1, 233068_at
Figure 1421: PRO84097
Figure 1422: DNA287404, AK026486, 233085_s_at
Figure 1423: PRO69661
Figure 1424: DNA331422, 077853.1, 233289_at
Figure 1425: PRO86485
Figure 1426: DNA331423, AF176071, 233467_s_at
Figure 1427: DNA329571, HSPC195, 233955_x_at
Figure 1428: PRO51662
Figure 1429: DNA331424, LOC112840, 235025_at
Figure 1430: PRO86486
Figure 1431: DNA330888, 7687712.2, 235088_at
Figure 1432: PRO69581
Figure 1433: DNA330891, AK027315, 235113_at
Figure 1434: PRO86052
Figure 1435A-C: DNA331425, 228001.3, 235116_at
Figure 1436: PRO20128
Figure 1437: DNA328146, BC019239, 235117_at
Figure 1438: PRO84051
Figure 1439: DNA330906, NP_116171.2, 235458_at
Figure 1440: PRO86067
Figure 1441: DNA194081, DNA194081, 235556_at
Figure 1442: PRO23477
Figure 1443: DNA330916, 234580.1, 235670_at
Figure 1444: PRO86077
Figure 1445: DNA330943, 1042935.2, 237009_at
Figure 1446: PRO86104
Figure 1447: DNA331426, 361450.1, 237542_at
Figure 1448: PRO86487
Figure 1449: DNA331427, AB052906, 238542_at
Figure 1450: PRO791
Figure 1451: DNA258952, DNA258952, 239901_at
Figure 1452: DNA328206, 1384214.3, 240277_at
Figure 1453: PRO84109
Figure 1454: DNA331428, 7692702.1, 241803_s_at
Figure 1455: PRO86488
Figure 1456: DNA329506, NP_387510.1, 241937_s_at
Figure 1457: PRO85067
Figure 1458: DNA331429, NP_110403.1, 242020_s_at
Figure 1459: PRO86489
Figure 1460: DNA331030, 407930.2, 242648_at
Figure 1461: PRO86188
Figure 1462: DNA331037, 206873.1, 242890_at
Figure 1463: PRO86195
Figure 1464: DNA329507, 407430.1, 242943_at
Figure 1465: PRO85068
Figure 1466: DNA331043, 005042.1, 243134_at
Figure 1467: PRO86201
Figure 1468: DNA331053, 243689.1, 243509_at
Figure 1469: PRO86211
Figure 1470: DNA331430, 030957.1, 243808_at
Figure 1471: PRO86490
Figure 1472: DNA331431, 201839.1, 243840_at
Figure 1473: PRO86491
Figure 1474: DNA331432, 151634.1, 244035_at
Figure 1475: PRO86492
Figure 1476: DNA331433, 020071.1, 244434_at
Figure 1477: PRO86493